

APPENDIX D

NONTECHNICAL ABSTRACT OF PROTOCOL

Many patients have advanced cancer that has not responded to standard therapies. For these patients, TIL (tumor infiltrating lymphocyte) therapy offers a new treatment protocol which has shown some encouraging results. In this therapy, a portion of the patient's tumor is removed and taken to the laboratory. In the laboratory the tumor portion is processed in a way to encourage the growth of white cells, called lymphocytes, which are found in (had infiltrated) the tumor. These tumor infiltrating lymphocytes are grown to large numbers in way that kills the cancer cells. These TIL are then infused back into the patient through a vein. These TIL are given with compounds, interleukin-2 and interleukin-4, which can enhance the anti-tumor immune response of the patient as well as the TIL.

TIL therapy has been shown to be effective in a fraction of patients receiving this therapy. At this time it is not known why some patients get a favorable response with TIL therapy and some patients do not. In order to further understand TIL therapy, it is important to be able to follow the TIL cells after they are given back to the patient. This way it will be possible to determine if the length of TIL survival or the ability of the TIL to "home" or return to the tumor is related to the response the patient experiences. Since the TIL are from the patient, there is no way to distinguish them from the other cells of the patient. In order to tell the TIL from the patient's other cells, a means to mark the cells is necessary. In other clinical tests with TIL it has been shown that the TIL can be marked. This marking involves the insertion of a new gene into a portion of the TIL cells by a technique called retroviral-mediated gene transfer. These marked TIL can therefore be detected by modern scientific techniques and distinguished from the patient's other cells.

The addition of a marker gene into a portion of the TIL will provide no immediate benefit for the patient. It would provide useful information about the therapy itself. This information may enable the design of better TIL treatment plans to help future patients. The risks associated with the gene marking procedure are minimal. The opportunity to learn more about TIL therapy so that future patients may be helped is the reason for using gene marked TIL.